REMARKS

In the first paragraph, on page 2 of the Office Action, the Examiner requests that Applicants amend the specification to update the status of the parent application as being issued U.S. Patent 6,340,574.

Accordingly Applicants hereby amend the specification as requested by the Examiner.

In addition, on page 2 of the Office Action, the Examiner objects to Figures 3 and 8A on the grounds that the figures are uninterpretable.

Applicants traverse the Examiner's objection.

First of all, Applicants respectfully submit that the results in Figures 3 and 8A are described in the present specification (see page 18, lines 4-6 and page 22, line 20 *et seq*), and hence clearly interpretable. Further, there is nothing in the actual figures which is essential to understanding the invention. Thus, Applicants submit that the Examiner's objection is improper.

Nonetheless, if the objection is not withdrawn, Applicants will submit additional copies of Figures 3 and 8A, or alternatively cancel these figures from the application.

On page 3 of the Office Action, the Examiner objects to the specification because, at page 4, line 14, SEQ ID NO:4 is not provided after "TATAA".

Accordingly, Applicants hereby amend the specification as requested by the Examiner, and thus request withdrawal of the Examiner's objection.

On page 4 of the Office Action, the Examiner rejects Claims 7-16 and 20-30 under 35 U.S.C. § 103 as being unpatentable over Mather et al in view of Efrat et al and Kushner et al.

Specifically, the Examiner states that it would have been obvious to modify the teachings of Mather et al with Efrat et al or Kushner et al to produce cells transfected with DNA encoding proteins required for survival under the control of a repressor gene. Further, the Examiner contends that one of ordinary skill in the art would have been motivated to do so because Mather et al teaches cells that can produce their own required factors, and further teaches that the required levels of these factors vary with the status of the cells; and Efrat et al and Kushner et al teach means by which the level of the factors produced by the cells can be varied.

For the following reasons, Applicants respectfully traverse the Examiner's rejection.

Mather et al discloses host cells which are transformed with a nucleic acid encoding a polypeptide factor required for its growth or survival and a nucleic acid encoding a desired protein, wherein the host cells can be grown in medium lacking the polypeptide factor. However, Mather et al does not teach or suggest host cells transformed with a nucleic acid encoding a polypeptide growth factor that is controlled by an inducible promoter, as claimed in the present invention. That is, in contrast with the present invention, Mather et al only teaches the use of constitutive promoters (see column 7, line 61 to column 8, line 7 thereof). Thus, Mather et al does not contemplate

switching on/off the expression of the polypeptide factor, as in the present invention.

Accordingly, Applicants respectfully submit that the present invention is not taught or suggested by Mather et al, and for the following reasons, it is clear that neither Efrat et al nor Kushner et al provide the deficiencies which exist therein.

Efrat et al discloses a conditionally transformed cell line derived from pancreatic β cells of transgenic mice. The transformed cell line contains the bacterial tetracycline resistance open regulatory system. In the presence of tetracycline, Tag oncoprotein expression is down-regulated and the cells undergo a reversible growth arrest. Notably, the cells require the presence of serum for their growth (see page 3577 under the heading "cell culture" in Materials and Methods). There is no "induced expression" of a polypeptide factor required for cell growth in the present invention.

Kushner et al discloses the use of the inducible metallothionein promoter family to control expression of a nucleic acid encoding a desired protein in mammalian host cells. There is, however, no teaching or suggestion therein of transforming a host cell with a nucleic acid encoding a polypeptide growth factor that is controlled by an inducible promoter, e.g., the metallothionein promoter, as claimed in the present invention.

Applicants note the Examiner's argument that Mather et al indicates that the amounts of the required polypeptide factors may need to be varied depending upon the needs of the particular host cell type, and for some polypeptide factors, that there may only be a need for them when the host cells are initially plated or

when the host cells are present in the culture at low density (see column 6, lines 45-62 thereof). However, there is no teaching or suggestion in Mather et al that such variations might be achieved by transforming the host cells with a nucleic acid encoding the required factor(s) that is controlled by an inducible promoter. In fact, Mather et al teaches alternative means for achieving variations in the amount of polypeptide factors. In particular, Mather et al refers to the use of enhancers to increase transcription from a constitutive promoter (see column 8, lines 8-26 thereof) and, for the case where the polypeptide factor is required only when the host cells are initially plated or when the host cells are present in the culture at low density, Mather et al teaches the following simple solutions: "pre-coat the dish with serum; plate cells in serum-containing medium for 12-24 hours and then change to serum-free; reduce serum concentrations to the point where the cells will survive but not grow; and use attachment factors" (see column 6, lines 56-62 thereof). In the light of these teachings, Mather et al clearly provides no motivation to use an inducible promoter system and, in fact, teaches away from use of such. Hence, the Examiner's rejection can only be made in hindsight, which is legally improper.

Furthermore, Mather et al does not envisage the advantage that may be achieved by the claimed method or host cell (i.e., that the host cell of the present invention, when further transformed with a nucleic acid encoding a desired protein, may be controlled to the extent that expression of the polypeptide growth factor can be restricted to the growth phase of the host cell, thereby providing a period during which the protein expression

burden of the host cell is reduced so as to allow for improved yield of the desired protein).

Accordingly, Applicants respectfully submit that the present invention is not taught or suggested by Mather et al alone and that the combination thereof with the teachings of Efrat et al and Kushner et al, can only be made in hindsight, which is legally improper. Thus, Applicants request withdrawal of the Examiner's rejection.

In view of the amendments to the specification and the arguments set forth above, reexamination, reconsideration and allowance are respectfully requested.

The Examiner is invited to contact the undersigned at his Washington telephone number on any questions which might arise.

Respectfully submitted,

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